The Relation between Low Birth Weight in Preterm Children and Their Attentional Abilities

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Abstract

Recent studies have shown that the preterm children present several neuropsychological deficits of varying severity (e.g. in visuospatial abilities, working memory, executive functioning etc and a reduced academic performance. These findings seem growing with decreasing of the gestational age (e.g. before the 32nd week of pregnancy) and/or the birth weight (e.g. ≤ 2400-1500 g). However birth weight has been revealed as the parameter more useful as a putative index of the Central Nervous System immaturity. The main objective of this study was to characterize the attentional abilities in a sample 7-years-old prematurely born children with a birth weight minor than 2400 g (N=51) in a comparison with a matched control group (N=46) of term children. With this aim, an adaptation of the Sohlberg and Mateer´s attention model including its five components: focused, sustained, selective, alternating and divided attention was used. The preterm group performed significantly worse than the control group in all evaluated attentional processes; and the birth weight showed an inversely proportional significant effect with respect to this neuropsychological test.

In conclusion, the attentional model proposed to assess this domain in preterm children has shown this efficiency to detect a generalized attentional deficit, even in tasks requiring the more basic components. These findings may account for some aspects of the cortical development and early brain organization.

Keywords

Preterm Birth; Birth Weight; Attention; Infant Neuropsychology

Introduction

According to the Spanish National Statistics Institute, in 2010 about 8% of children were born before 37 weeks of pregnancy (National Statistics Institute, 2012). Survival rates have greatly improved in recent years for infants of borderline viability; these babies, however, remain at risk of causing a wide array of complications, not only in the hospital neonatal units, but also in the long term, throughout the period from infancy to adulthood (S. Saigal, 2000). These consequences include motor disorders, visual deficits and other kinds of sensorial disabilities, cognitive and learning difficulties, as well as behavioral (e.g. poor inhibition and attentional control), emotional and social problems [(M. Colvin, 2004), (H. Mulder, 2010)].

These findings increase when referred to the very preterm —VPT— children. As well as the general preterm children population, VPT children have been defined in regard with the gestational age (e.g. born before the 32th week of pregnancy) and/or the birth weight (e.g. ≤ 1500 g). Thereby several studies have shown that over 50% of children born before the 28th week of pregnancy presents cognitive deficits and reduced academic performance, which demands additional support during their education [(H. Mulder, 2010), (A. Burguet, 2000), (P. Olsén,, 1998), (J. W. Pasman, 1998), (B. S. Peterson, 2000)]. At the same time, children with very low birth weight also have a higher rate of learning difficulties, behavioral disorders and health problems than children born with a normal weight (G. P. Aylward, 2005). Therefore, a substantial proportion of VPT children develops cognitive deficit and abnormal behaviors during infancy (A. T. Bhutta, 2002).

A disruption of brain development and neural organization may account for the multiple functional

impairments observed in the VPT population. Indeed, reduced cortical and subcortical gray and white matters volumes in VPT children have been documented [(B. S. Peterson, 2000), (G. P. Aylward, 2005), (B.S. Peterson, 2003)]. Disturbance of critical stages of brain development is particularly associated with births previous to the 33th week of pregnancy and may be partially explained by an increased vulnerability to inflammation and/or neuronal death due to developmentally unexpected harmful events, such as stress, neonatal pain, maternal separation during intensive care, increased auditory/visual stimulation and sleep deprivation (R. W. Hall, 2008). Thus, it seems that premature birth is associated with an alteration of brain development, and it would result in persistent disturbances of perceptive, executive, mnesic and attention abilities (B. H. Esbjorn, 2006).

Attentional disturbances achieve a predominant significance in behavioral, clinical and academic domains, as several studies have revealed that VPT children show attention-related disorders, including attention deficit hyperactivity disorders (ADHD). Indeed, ADHD is the most frequent behavioral syndrome diagnosed in VPT children. Suggestive symptoms of ADHD are reported to occur at 2.6 to 4 times more frequently in VPT children than in controls; therefore, between 16% and 47% of VPT children have symptoms of ADHD in childhood and adolescence [9]. This outcome can be largely predicted from neonatal white matter injuries, as well as from parenchymal lesions and ventricular enlargements associated with premature birth (S. Johnson. Semin, 2007). Hence, VPT children could be singularly prone to attentional deficits that may also be responsible for their reduced competence in other cognitive domains.

However, attention is not a general property of the whole brain. Neuroimaging studies have shown that specific networks of neural areas are involved in several functions related to attention (M. I. Posner, 2006). The previous literatures have been documented that VPT children have difficulties in attentional shifting and inhibitory processes [(B. H. Esbjorn, 2006), (M. I. Posner, 2006)], but those studies have not systematically assessed whether this population exhibits a general executive deficit or rather an alteration of specific components of this complex cognitive function.

The clinical model of attention proposed by Sohlberg and Mateer (M. M. Sohlberg, 1987) could be a useful tool to get to know attentional capabilities in VPT children. Although the Attention Process Training program was designed to improve the attention in specific brain injury patients (i.e. traumatic brain injury), it is based on a model of attentional functioning which divides this domain in five different components: focused, sustained, selective, alternating and divided attention. We believe that this model could be useful not only to differentiate what attentional aspects are alter in preterm children but also to know how to classify them hierarchically: we believe that the more complex attentional factors according to this model (e.g., alternating and divided attention) will be in deficit in all preterm children.

In the context ofthe context of an investigation about the neuropsychological development in a sample of preterm children, we selected a set of attentional tasks that could valuate the different components of the Sohlberg and Mateer model pointed out before, according to previous studies (B. Lopez-Luengo, 2003) and classic handbooks on neuropsychological assessment (M. D. Lezak, 2004). This protocol of evaluation could show its usefulness because it makes feasible the monitoring of any possible improvement detected in longitudinal studies concerning the attentional abilities of these children.

This study was conducted in a sample of 7-years-old preterm children. By choosing this age period, it not only ensured sample homogeneity, but also made sure that all subjects had already acquired the reading and writing abilities required for the neuropsychological evaluation. Therefore, it is a known fact that maturation of axon sprouts occurs between 7 and 9 years old, and it is linked with the process of myelinization and synaptogenesis (M. B. Jurado, 2007). At this age, there is a great increase in the activity of frontal regions, as well as an integration of the long distance connection located in the right hemisphere. In this period, children are able to manage information coming from different parts of the brain at the same time. This coordination requires a wide myelinisation and an increase in the production of neurotransmitters (E. Pérez, 2008).

Further, in our attempt to link attentional disabilities and Central Nervous System (CNS) immaturity to preterm group (PTG) children, subjects were classified into three groups according to their body birth weight: below 1500 g (very low weight group —VLWG—), between 1501 and 2400 g (low weight group —LWG—), and above 2401 g (control group —CG—), which roughly correspons to the weights classification used

in anterior studies [(G. P. Aylward, 2005), (P. H. Casey. Semin, 2008)]. According to the previous hypothesis, we consider that the wide range of attentional alterations, including the simplest components of the domain, will be manifested in low-weight children, while accepting the fact that this low weight is closely related to the immaturity of the CNS.

Methods

Sample

A retrospective study was designed by selecting a sample of 51 preterm children who represent 83% of premature children born during the 2000-01years at Torrecárdenas Hospital (Almería, Spain). Gender distribution was 71.4% males and 26.6% females. About the birth weight, 31 of these children were included in the VPTG (born at 32 weeks or less and/or with a weight lower than 1500 g) the remaining 19 children belonged to the PTG (between 1501-2400 g and/or born at 32 weeks). All of them underwent complete physical and neurological examination. Figures on the main neuroimaging results and physical diagnosis of these children are shown in Table 1.

The control sample, with more than 38 weeks of gestation and more than 2401 g of weight, comprised a similar number of children (N=46) matched in age, gender and education level with the clinical group. The educational level of parents was compared with that belonging to the parents of the preterm group.

TABLE 1 NEUROIMAGING IN THE PRETERM GROUP

Exam	Data	
	CNS injury detected	% PTG
NMR	Periventricular leukomalacia	6.3% (left) 15% (right)
PUS	Horn expanded Intraventricular haemorrhage	6.3 % (posterior) 18.8%

Abbreviations: CNS: Central nervous system; PTG: preterm group; NMR: Nuclear magnetic resonance; PUS: Postnatal ultrasonography.

The cases excluded from both samples were those presenting serious mental, psychological and sensorimotor deficiencies (established according to medical and physiotherapy criteria), which can imply a handicap at the time of comprehending or carrying out the tests. The study has approved by the Hospital Research Commission. It was conducted in accordance with the Helsinki declaration for biomedical research. Parents were informed in advance about the aims and procedures of the work, giving written informed consent and children were fully free to leave the study at any time.

Neuropsychological Evaluation

With the aim of detecting severely learning disabilities or mental retardation in the individuals of the sample, all children completed the Spanish adaptation of the *Kaufman Assessment Battery for Children* (*K-ABC*) (A. S. Kaufman, 1997). The *K-ABC* is a test of intelligence and achievement, based on neuropsychological and information-processing theories. Intelligence —or problem-solving abilities— is measured on two mental processing scales. One is the sequential processing scale, in which the child processes information serially or temporally in a stepwise fashion and, the other is the simultaneous processing scale, in which the child is required to solve problems that are analogical, spatial or organizational in nature. A mental processing composite scale is a unification of the sequential and simultaneous processing scales and is intended to measure total intelligence.

Besides, a measure of compressive language and its corresponding mental age were included using the *Peabody Picture* Vocabulary *Test* (*PPVT*) (L. M. Dunn, 1986). This test was preferred against other alternative measures because it is widely used as control assessment in typical studies on child neuropsychology [(E. H. Myers, 2010), (L. S. Siegel, 1983)]. The scaled scores were registered.

And with regarding of the attention domain, the neuropsychological assessment protocol was designed to cover the five increasingly demanding components of attention described by Sohlberg and Mateer (M. M. Sohlberg, 1987), but adapting their evaluation to children capabilities. More specifically, the selected tests were: Symbol Search and Cancellation, subtests included in the *Weschler Intelligence Scale for Children-fourth edition —WISC-IV—* (D. Wechsler, 2005), for the assessment of focused attention; Digit Span subtest (*WISC*-IV), Number Recall, Word Order and Hand Movements all of the subtest of the *K-ABC* for the assessment of sustained attention; *"A" Cancelation Test* —auditory version— (R. L. Strub, 2000) and *Stroop Color and Word Test* —Stroop Test—(C. J. Golden, 1987) for the assessment of selective attention; *Trail Making Test* part A and part B (Adjutant General's Office, 1944)

and Letter-Number Sequencing subtest (*WISC-IV*) for the assessment of alternating and divided attention. Scale score were obtained for *K-ABC* and *WISC-IV* tests. An interference scale score was registered in the Stroop Test according to the criterion of the Spanish adaptation of the task (C. J. Golden, 1987). Finally, a qualitative type measure (correct/not correct realization of the test) was selected for the "A" *Cancellation Test* and the *Trail Making Test*. The execution time of the task was also recorded in this last test.

Neuropsychological assessment was carried out in two 60-minute sessions.

Statistical Analysis

Statistical analyses were conducted in a two-step approach. At the first step, group's mean values (PTG vs. CG) of each test were calculated and compared by means of analysis of variance (ANOVA). In the second step, we tried to explore the relationship between the performance in those tests and body birth weight. This was accomplished by stratifying subjects in the three referred groups (VLWG: ≤ 1500 g; LWG: between 1501 g and 2400 g; and CG: ≤ 2401 g) trough a multivariate analysis of variance (MANOVA) that took into account all tests to assess the five attentional components simultaneously. Pillai's multivariate index was used to obtain the *F* value and corresponding probability values among the differences of the groups reported in each test, and which were regarded as significant if they were equal or lower than 0.05. We also used a trend analysis to determine the possible relationships between the neuropsychological performance and the status of prematurity, which was stratified in the three levels of body birth weight described above. Linear and quadratic trends were tested for each dependent variable. Post-hoc comparisons among three levels of averages of the weight variable, using the statistical test of least significant difference (LSD), completed the analyses.

An analysis concerning the interaction between birth weight and gestational age (weeks of gestation) was conducted using the general variance model. Such analysis was not included in this study since it did not yield significant outcomes.

Results

The absence of differences between groups regarding socio-demographic variables was used as the criteria to select the participants of the present study. The results obtained from both groups were comparable with regard to age and educational level.

Results concerning the mental processing composite scale of the *K-ABC*, as a way to estimate Intelligence Quotient (IQ), show there are no significant differences among the groups of this scale with regard to birth weight variable (F(2,94) =2.27, MSE =536.80, p =0.106), gestational age variable ($F(2,94)$ =0.064, MSE =14.93, p =0.938) or the interaction between both ($F(2,94)$ =0.007, MSE =1.59, p =0.934). Marginal analyses, though, do reveal differences between groups with regard to birth weight. As for this case, the group with a weight over 2401 g shows significantly better scores than the rest (CG vs. VLWG: LSD =23.452, p =0.00; CG vs. LWG: LSD =19.10, p =0.00).

Conversely, both groups (PTG and CG) differed significantly in their scores with reference to each single selected test (see Table 2). In addition, the PTG exhibited scores below the normality cut-off point of their normative population in all these measures, except in the case of the Symbol Search subtest and the Stroop Test.

In the second step, MANOVA revealed that body birth weight was related to the value of subjects' performance, according to Pillai's criterion on weight (Pillai =108.00, p =0.004), as well as a significant difference with respect to all the tests concerning neuropsychological evaluation. A subsequent detailed trend analysis revealed that there was in fact a strong linear relationship between body birth weight and performance in almost all tests measuring different attention processes. This is the case of the results of the *PPVT* ($F(2,94)$ =14.012, MSE =57.858, p <0.001), the quality of performance of *Trail Making Test* part A and part B ($F(2,94)$ =11.695, MSE =0.903, p =0.001; $F(2,94)$ =19.025, MSE =2.355, p <0.001, respectively), the time of performance of both *Trail Making Test* part A and B ($F(2, 94)$ =9.29, MSE =24076.319, p =0.003; $F(2,94)$ =11.07, MSE =40490.043, p =0.001), the "A" *Cancellation Test* ($F(2,94)$ =9.72, MSE =0.983, p =0.002), and the following subtests of the *WISC-IV*: Cancellation ($F(2,94)$ =13.86, MSE =0.505, p <0.001), Digit Forward ($F(2,94)$ =18.81, MSE =20.39, p <0.001) and the Symbols Search ($F(2,94)$ =14.99, MSE =133.835, p =0.00). The subtests of Number Recall, Word Order and Hand Movements of *K-ABC* were also significant in relation to the linear trend ($F(2,94)$ =12.62, MSE =100.091, p =0.001; $F(2,94)$ =20.25, MSE =110.506, p <0.001and $F(2,94)$ =16.71, MSE =124.314, p <0.001, respectively). The only exceptions of this general trend included Letters-Numbers

Sequencing subtest, in which both the linear trend and the quadratic trend were significant ($F(2,92)$ =64.08, MSE =843.311, p <0.001; $F(2,94)$ =5.97, MSE =78.673, p =0.016, respectively) and the Stroop Test ($F(2,94)$ =1.99, MSE =336.087, p =0.14), which apparently followed a linear trend but did not report any statistical significance.

TABLE 2 MEAN, STANDARD DEVIATION (SD), AND THE RESULTS OF F TESTS WITH THE ASSOCIATED PROBABILITY FOR THE CONTROL AND PRETERM GROUP IN THE ATTENTIONAL DOMAIN (*P <0.05; **P <0.01; ***P <0.001)

Function	Test	PTG	CG	F
Language	*PPVT*	9.91 (2.2)	10.55 (2.1)	14.01***
Attention				
Focused	Symbol Search (*WISC-IV*)	10.26 (3.35)	12.28 (2.7)	14.99***
	Cancellation (*WISC-IV*)	7.85 (3.71)	10.42 (2.85)	13.86***
Sustained	Digit Span forward (*WISC-IV*)	3.63 (1.55)	4.83 (1.37)	18.81***
Selective	"A" Cancellation Test	0.77 (0.42)	0.97 (0.14)	9.72**
Alternating and divided	Trail Making Test A (quality)	0.81 (0.39)	1 (0.0)	11.70***
	Trail Making Test A (time)	128.63 (63.27)	92.47 (38.03)	9.29**
	Trail Making Test B (quality)	0.67 (0.47)	0.97 (0.14)	19.03***
	Trail Making Test B (time)	217.89 (70.78)	172.52 (48.78)	11.07***
	Letter-Number Sequencing (*WISC-IV*)	7.55 (4.39)	13.61 (2.88)	64.08***

Abbreviations: PTG: Preterm group; CG: Control group; *PPVT*: Peabody picture vocabulary test; *WISC-IV*: Wechsler intelligence scale for children-fourth eidtion.

On the other hand, LSD-based mean comparisons revealed that groups differed among them in all tests. In most cases (except for the *PPVT* and Stroop test), differences were maximal when comparing the high-weight group with the other (see Table 3). As for *PPVT*, the three weight groups show differences among them, which as the results reported by the Stroop Test (F (2,94) =1.99, p =0.14) could be due to the great variability in the low-weight groups (VLWG: Mean =45.18, SD =17.97; LWG: Mean = 46.78, SD = 16.77) with respect to the CG, the higher weight group (Mean = 50.93, SD = 4.22); also a detailed analysis of this variability and the component of the task (word and cross reading, and interference conditions) should be studied in different samples.

TABLE 3 RESULTS OF LEAST SIGNIFICANT DIFFERENCES (LSD) BETWEEN DIFFERENT GROUPS OF BIRTH WEIGHT IN THE NEUROPSYCHOLOGICAL TESTS SCORES (*P <0.05; **P <0.01; ***P <0.001)

Function	Test	Weight groups		LSD
Language	*PPVT*	VLWG	LWG	-1.19*
			CG	-1.76***
		LWG	VLWG	1.19*
		CG	VLWG	1.76***
Attention				
Focused	Symbol Search (*WISC-IV*)	VLWG	CG	-2.67***
		CG	VLWG	2.66***
	Cancellation (*WISC-IV*)	VLWG	CG	-2.82***
		LWG	CG	-2.95***
		CG	VLWG	2.82***
			LWG	2.94***
Sustained	Digit Span backward (*WISC-IV*)	VLWG	CG	-1.45***
		LWG	CG	-0.84*
		CG	VLWG	1.45***
			LWG	0.84*
	Number Recall (*K-ABC*)	VLWG	CG	-2.30***
		LWG	CG	-2.36**
		CG	VLWG	2.30***
			LWG	2.36**
	Word Order (*K-ABC*)	VLWG	CG	-2.42***
		LWG	CG	-2.25***
		CG	VLWG	2.42***
			LWG	2.25***
	Hand Movements (*K-ABC*)	VLWG	CG	-2.57***
		LWG	CG	-2.32**
		CG	VLWG	2.57***
			LWG	2.32**
Selective	"A" Cancellation Test	VLWG	CG	-0.23**
		CG	VLWG	0.23**
Alternating and divided	Trail Making Test A (quality)	VLWG	CG	-0.22**
		CG	VLWG	0.22**
	Trail Making Test A (time)	VLWG	CG	35.88**
		LWG	CG	55.49***
		CG	VLWG	-35.88**
			LWG	-55.49***
	Trail Making Test B (quality)	VLWG	CG	-0.35***
		CG	VLWG	0.35***
	Trail Making Test B (time)	VLWG	CG	46.53***
		LWG	CG	56.95***
		CG	VLWG	-46.53***
			LWG	-56.95***
	Letter-Number Sequencing (*WISC-IV*)	VLWG	CG	-6.68***
		LWG	CG	-5.62***
		CG	VLWG	6.68***
			LWG	5.62***

Abbreviations: VLWG: Very low weight group; LWG: Low weight group; CG: Control group; *PPVT*: Peabody picture vocabulary test; *WISC-IV*: Wechsler intelligence scale for children-fourth eidtion; *K-ABC*: Kaufman assessment battery for children.

Discusion

In the present study we evaluated the attentional abilities of 7-years-old very prematurely born children. To better characterize the possibility of attentional deficits in this population, we performed this assessment according to the model of Sohlberg and Mateer (M. M. Sohlberg, 1987) which distinguishes five major components of attention, namely, focused, sustained, selective, alternating and divided attention. Results showed significant differences between VPT children and a term born children in all the attentional tests, and a strong linear trend between these attentional abilities and CNS immaturity, as inferred from body birth weight.

Previous studies had evinced that VPT children displayed a poor performance in selective attention tasks (N. Breslau, 1996), sustained attention and set shifting tasks (H. G. Taylor, 1998) as well as a reduced working memory, selective attention and attention shifting abilities (D. Shum, 2008). Recently, Pizzo et al. (R. Pizzo, 2010) have shown a specific deficit in executive control abilities in preterm children. Therefore, the present study confirms and extends these results, pointing out that VPT children display attentional deficits even in the lowest levels of the hierarchical attention model proposed by Sohlberg and Mateer, thus suggesting that VPT children present a generalized deficit in this cognitive domain.

On the other hand, previous studies had revealed an inverse correlation between cognitive performance and body birth weight [(A. T. Bhutta, 2002), (S. Johnson, 2007), (H. G. Taylor, 1998)], emphasizing the developmental vulnerability of an immature brain. In our case, we also found that the lower the body weight was, the poorer the cognitive performance was. Furthermore, more detailed analyses show that the cut-off points in all the attentional levels are mainly detected in children with less than 2400 g of weight. So, we can consider that below this weight, children's brains are not sufficiently mature to perform these cognitive skills, or there may be other unknown factors in low weight children that can explain these results, such as alterations in the regulation of several neurotransmitters, or disturbances in the cognitive networks (L. R. Ment, 2003).

A generalized attention deficit, as the one identified in the present study, could also probably account for the behavioral and cognitive disturbances of prematurely born children during adulthood. More specifically, it can be hypothesized that the brains of VPT children are not just delayed in their maturation, but rather unable to reach a normal cognitive development permanently. Indeed, several studies have pointed out that 15-47% of VPT children have ADHD symptoms [(G. P. Aylward, 2005), (A. T. Bhutta, 2002), (S. Johnson, 2007)] and other behavior disorders, unassertiveness, impulsivity, anxiety and social skills deficits also occur more frequently in VPT than in their non-VPT peers. These disturbances could be linked to a disruption of frontal-striatal-thalamic circuits implicated in attention and executive functions.

The significance of our outcomes lies in the employment of the procedure within the sphere of rehabilitation. The number of studies dealing with results obtained from rehabilitation techniques on premature children is quite small [(M. C. McCormick, 2006), (C. Pisaturo, 1990)]. While the neuropsychological intervention (cognitive and behavioral) is crucial on account of the school, academic and labor repercussions in these children [(S. Johnson, 2007), (E. T. Hille, 2007)] do not seem relevant. Data concerning the aforementioned studies exhibit some progress in the cognitive and motor capacities of preterm children; although these data do not reach the values found in the control group of healthy and full term children [36]. Probably, the most relevant study (with regard to the individuals of the sample and the number of measures observed) has been carried out by McCormick and his team (M. C. McCormick, 2006). The study reports that those preterm children (a birth weight over 2000 g) who are put under the Infant Health and Development Program obtained better scores, in the short and long term, in tests assessing education and cognitive achievements. However, it is worth bearing in mind that those preterm children with a birth weight below 2000 g do exhibit neither continuity nor generalization of achieved progresses and after some time (2 years) the progress disappears.

When we look at the results of our study, we note a linear relation between birth weight and the execution of attentional tasks, so that VPT children, with a birth weight below 1500 g, get lower scores than the rest of the groups. The involvements associated to the intervention are of extreme significance when we bear in mind the conclusions reported by McCormick et al. (M. C. McCormick, 2006) therefore, the follow-up and the intervention in VPT children, with a birth weight below 1500 g, must be continuous, close and in the long term.

Conclusions

In conclusion, we have evinced that VPT children showed a generalized attentional deficit which affects even the most basic components of this cognitive function, such as focused and sustained attention. This deficit is strongly related to the body weight of the children at birth. A lower body birth weight worsens their performance in any attentional task, regardless of the evaluated degree of complexity of the attentional component In addition, it is observed that the cut-off point to establish the criterion of normality is at 2400 g. Bellow this level, subjects generally show attentional disturbances.

Also, we have displayed the utility of the attentional model of Sohlberg and Mateer (M. M. Sohlberg, 1987). Although, this model was not developed for clinical evaluation, but as a rehabilitation tool, its utility has been well exhibited in this study. Further studies are needed to shed light on the relationship between body weight at birth, a datum that seems to be a useful index of CNS maturity and behavioral and cognitive deficits. This kind of knowledge could be very helpful in the attempt to design specific evaluation/training programs to assess/exploit the putative reversibility of such deficits.

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